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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,892	05/17/2005	Braj B. Lohray	4062-126	1055

23117 7590 03/17/2008
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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
03/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,892	LOHRAY ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *9,10,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-15 and 18-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/1/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I in the reply filed on 1/9/2008 is acknowledged. The traversal is on the ground(s) that the restriction is improper. This is not found persuasive because the methods are patentably distinct. Treatment of toxicity due to chemotherapy is patentably different from treatment of bacterial infections, psoriasis, or arthritis.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claims 1-3 and 5-8 are objected to because of the following informalities: they contain non-elected subject matter. Appropriate correction is required. Claim 21 is objected to because it contains three periods, which makes it difficult to determine the beginning and ending of the claim. In addition claim 21 is difficult to read (the first reactant of part iiii is unclear).

Specification

3. The abstract of the disclosure is objected to because it is not descriptive of what has actually been invented. Correction is required. See MPEP § 608.01(b).

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-8, 11-15, and 18-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salts and tautomeric forms of the elected group of compounds, does not reasonably provide enablement for analogs, solvates, derivatives, and

prodrugs of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Applicants show that a salt of formula I can be made, as well as tautomeric forms of formula I (where variable W is $NHC(X)R^7$. Applicants do not teach preparation of any solvate or prodrug of formula I. Vippagunta et al. (*Advanced Drug Delivery Reviews*, **2001**, *48*, 3-26) teach that solvate formation is unpredictable (page 18 section 3.4). Janzten and Robinson (*Modern Pharmaceutics*, **1996,** page 596) show that prodrug development requires undue experimentation, in the identification of a correct substituent and in the testing required for safety and efficacy. Since either a prodrug or a solvate can each be considered an analog or derivative, these forms of the compound are not enabled as well.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to antibacterial compounds that are composed of three different ring systems, a phenyl ring, a piperazine ring, and an oxazolidinone ring.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The prior art shows that solvate formation is unpredictable and prodrug development requires undue experimentation.

(5) The relative skill of those in the art:

One of ordinary skill in the art is familiar with the synthetic techniques used in the specification.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for formation of salts or tautomers.

However, the specification does not provide guidance for formation of derivatives, analogs, prodrugs, and solvates.

(8) The quantity of experimentation necessary:

Prodrug testing requires extensive testing for safety and efficacy.

Considering the state of the art as discussed by the references above, particularly with regards to claims 1-8, 11-15, and 18-22, and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

7. Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of bacterial infections associated with *Methicillin resistant Staphylococcus aureus* 6538P, *Staphylococcus epidermis* ATCC 12228, *Enterococcus faecaelis* ATCC 29212, *and Staphylococcus aureus* ATCC 33591, does not reasonably provide enablement for treatment of a disorder associated with any other bacteria. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicants show that prepared compounds inhibit the specified bacteria *in vitro* (page 64, table on bottom of page). Genin (*Expert Opinion in Therapeutic Patents*, **2000**, *10(9)*, 1405-14) shows that bacterial infections are linked with psoriasis and arthritis.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to a method of inhibiting bacterial growth with compounds that are composed of three different ring systems, a phenyl ring, a piperazine ring, and an oxazolidinone ring.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The prior art shows that bacterial infections are linked to psoriasis and arthritis.

(5) The relative skill of those in the art:

One of ordinary skill in the art is familiar with the assays used in the specification.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for inhibition of *Methicillin resistant Staphylococcus aureus* 6538P, *Staphylococcus epidermis* ATCC 12228, *Enterococcus faecaelis* ATCC 29212, *and Staphylococcus aureus* ATCC 33591.

However, the specification does not provide guidance for inhibition of any other bacteria.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 7-8, and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-8, 11-15, and 18-22 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Is claim 1 a compound claim or a composition claim? Both are present in the preamble of said claim. The "thio" group for variables R^1 through R^4 appears to be a dangling valence. What is the sulfur atom attached to? What groups act as substituents for alkyl, aralkyl, alkoxy, thio, amino, aminoalkyl, thioalkoxy, cycloalkyl, haloalkyl, and haloalkoxy groups of variables R^1 and R^2? What groups act as substituents for cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, acyl, acyloxy, carboxylic acids and derivatives, and every other substituted group for variables R^3 and R^4? If the dotted line of page 66 represents a bond, then groups G_2 and G_3 can only have two variables attached (because it will be an alkyne). What type of bacterial infection(s) is/are being treated in claims 7-8? MeSH shows various types ("Bacterial infections", http://www.nlm.nih.gov/cgi/mesh/2008/MB_cgi, accessed 2/7/2008). In claim 21, to what is the phrase "as defined earlier" referring to?

10. Regarding claim 1, the phrase "such as" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

11. Regarding claim 22, the phrase "etc." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

12. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: each of the processes in claim 22 is missing required elements. For example, in step D, how is the azide being converted to a primary amine. In step B, how is the hydroxyl group being converted to a leaving group before the nucleophilic attack of L? What solvents are present in each of these processes? Processes E, F, G, and H are all missing the required reactants to perform the reaction..

Oath/Declaration

13. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

14. Duplicate Claims

15. Claim 6 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim

to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Since claim 1 is both a compound claim and a composition claim and claim 6 is a composition claims, these claims are substantial duplicates.

16. Claim 18 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 6. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). In the instant case, both compounds are composition claims. A medicine is considered a composition. Thus, claim 18 is a duplicate of claim 6.

Allowable Subject Matter

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner
Art Unit 1624

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